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Guidance for Industry and FDA Staff

510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device

DRAFT GUIDANCE

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On July 28, 2011 this document was edited to correct a typo on P.5.

For questions regarding the use or interpretation of this guidance in the review of submissions to the Center for Devices and Radiological Health, contact Michael J. Ryan at 301-796-6283 or by email at michael.ryan@fda.hhs.gov.

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When final, this document will supersede *Deciding When to Submit a 510(k) for a Change to an Existing Device*, dated January 10, 1997.



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Food and Drug Administration
Center for Devices and Radiological Health**

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Preface

Public Comment

Written comments and suggestions may be submitted at any time for FDA (Agency) consideration to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, refer to Docket No. FDA-2011-D-0453. Comments may not be acted upon by the Agency until the document is next revised or updated.

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Guidance for Industry and FDA Staff

510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. Introduction

FDA developed this draft document to provide guidance to manufacturers on when to submit a premarket notification submission (510(k)) for changes or modifications made to that manufacturer's¹ previously cleared medical device. The underlying principles that FDA uses to determine when a 510(k) is necessary for a modified device are explained here, and examples are provided for additional clarity. When final, this guidance will supersede the 1997 version of the guidance document, [Deciding When to Submit a 510\(k\) for a Change to an Existing Device](#).

In 2010, FDA initiated a review of its process for premarket review of medical devices and undertook two significant initiatives to improve the Agency's medical device premarket review programs. In August 2010, FDA released two reports, including the analyses and recommendations that suggested changes were needed to improve the predictability, consistency, and transparency of these programs. After receiving input from industry, stakeholders and the public, in January 2011, FDA announced 25 specific actions that the Agency will take to improve the premarket review programs. Updating the 1997 version of the guidance document, [Deciding When to Submit a 510\(k\) for a Change to an Existing Device](#), is one of these actions.

The recommendations in this draft guidance document are consistent with FDA policy for when a modification to a device does – and does not – require the submission of a 510(k).

¹ For the purposes of this document, the term "manufacturer" includes any 510(k) holder, even if that person does not actually fabricate the existing device. The term also includes persons who market a preamendments device (a device legally marketed in the US prior to May 28, 1976) or a device that is currently exempt from the 510(k) requirements of the FD&C Act.

The guidance has been updated, however, to address issues associated with software and other rapidly changing technologies, and to provide greater clarity about changes that do not trigger the need for a new premarket submission. This guidance uses examples of modifications to devices involving such technologies to illustrate changes that require a new 510(k), and changes that may simply be documented in accordance with a manufacturer's existing Quality System without prompting the need for a new 510(k) submission. FDA believes increased certainty about the regulatory consequences of device modifications is critical to facilitating advancements in device technology.

FDA's guidance documents, including this one, do not establish legally enforceable responsibilities. Instead, guidance documents describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in Agency guidance documents means that something is suggested or recommended, but not required.

II. Background

21 CFR 807.81(a)(3)

Almost from the 1976 enactment of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act (the FD&C Act), FDA has attempted to define with greater clarity when a modification to an existing medical device would – or would not – trigger the requirement that a new 510(k) be submitted to the Agency and cleared prior to marketing of the modified device. FDA regulations (21 CFR 807.81(a)(3)) state that a 510(k) must be submitted when:

(3) The device is one that the person currently has in commercial distribution or is reintroducing into commercial distribution, but that is about to be significantly changed or modified in design, components, method of manufacture, or intended use. The following constitute significant changes that require a premarket notification:

- (i) A change or modification in the device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process.
- (ii) A major change or modification in the intended use of the device.

FDA issued the original guidance document *Deciding When to Submit a 510(k) for a Change to an Existing 510(k)* in 1997 to clarify the language used in this regulation, particularly the phrase "could significantly affect the safety or effectiveness" and use of the adjectives "major" and "significant." Since then, regulatory changes such as the implementation of the Quality System regulation (21 CFR part 820) have occurred, and medical device technology has evolved. Accordingly, FDA is issuing this draft, updated guidance to reflect the Agency's current thinking and emphasize the most important factors in determining whether to submit a 510(k) for a device modification.

Changes that "Could Significantly Affect" Safety or Effectiveness

The regulation, 21 CFR 807.81(a)(3), requires a new 510(k) for any change or modification that “could significantly affect” either the safety or the effectiveness of a device. Whether a change could *significantly* affect the safety or effectiveness of a device is the key issue this guidance tries to address. It is important to note that device changes intended as improvements to a device’s safety or effectiveness could significantly affect the safety or effectiveness and require a new 510(k).

It is also important to note that the question addressed by this guidance is a different question from whether a change *does* significantly affect the safety or effectiveness of a device. Whether a change *does* affect safety and effectiveness is typically demonstrated by testing submitted in a 510(k) application. In most cases testing cannot, however, conclusively show that a change could not affect safety or effectiveness. We have developed this draft guidance to categorize the types of changes likely to require new 510(k) submissions, the types of changes that generally do not require new submissions, and to identify gray areas where we recommend sponsors speak to the agency before determining whether a new 510(k) should be submitted.

“A Major Change or Modification in the Intended Use” of a Device

Section 513(i) of the FD&C Act provides that a device may only be found substantially equivalent to a legally marketed predicate device if, among other things, the device has the same intended use as the predicate device. Thus, if a device modification results in a new intended use for the device, the Agency must find the device to be not substantially equivalent (NSE) and the device will require premarket approval. Changes to the indications for use, however, do not necessarily constitute a new intended use that would render the device NSE and trigger the requirement for a PMA. However, because changes to the indications for use are generally “major” changes to the intended use under 807.81(a)(3), they generally will require submission of a new 510(k). To clarify this principle, this guidance identifies several specific labeling changes or device modifications that affect the indications for use in a way that they have a major impact on intended use and thus require the submission of a 510(k).

III. Scope

This guidance applies to devices that are subject to premarket notification requirements. This guidance does not address issues unique to combination products, although the principles discussed in this guidance may be applied to submissions for combination products on a case-by-case basis. Contact the Office of Combination Products (OCP) for information on combination products at 301-796-8930 or combination@fda.gov. Furthermore, this guidance is not intended to address the need for submitting 510(k)s by manufacturers² of devices for which they do not hold the 510(k).³

² 21 CFR 820.3(w): “Remanufacturer means any person who processes, conditions, renovates, repackages, restores, or does any other act to a finished device that significantly changes the finished device’s performance or safety specifications, or intended use.”

³ See, for example, [Guidance for Industry and FDA Reviewers - Reprocessing and Reuse of Single-Use Devices](#) and [Frequently-Asked-Questions about the Reprocessing and Reuse of Single-Use Devices by Third-Party and Hospital Reprocessors](#)

The types of modifications addressed in this draft guidance include manufacturing process changes, labeling changes, technology or performance specification changes, and materials changes. This guidance is intended to assist industry in determining whether a new 510(k) is submission is necessary whenever a manufacturer makes a change to its own legally marketed device. This guidance may be used to determine whether device modifications made as corrective actions in recall situations warrant a new 510(k) submission. (See the Blue Book Memorandum K95-1, [510\(k\) Requirements During Firm-Initiated Recalls](#); if a correction alters a device rather than simply restoring it to its original specifications, a new 510(k) may be necessary. This guidance may be useful in determining whether one is warranted in cases where the correction does alter the device.)

This draft guidance document incorporates existing guidance and policy⁴ regarding when 510(k)s are necessary for modifications to legally marketed devices. In some cases, the existing guidance derives from advice given to only a few manufacturers for a limited number of devices. In such instances, we have attempted to generalize the concepts to apply to a broader range of devices. However, special cases exist where both manufacturers and FDA have worked to establish guidance for modifications to specific devices, e.g., daily wear contact lenses (see [Premarket Notification \(510\(k\)\) Guidance Document for Daily Wear Contact Lenses](#)). This draft guidance is not intended to supplant such existing device-specific guidance but may cover areas not addressed in those device-specific guidances. This draft guidance is also not meant to supersede the Office of In Vitro Diagnostic Device Evaluation and Safety's (OIVD) [Guidance for Industry and FDA Staff; Replacement Reagent and Instrument Family Policy](#).

The questions and answers in the following sections are provided as guidance to help manufacturers in determining whether a new 510(k) is necessary for a change or modification to an existing device. Manufacturers make the initial determination of whether a device modification requires a new 510(k), while FDA staff may review these decisions during post-market inspections. These questions should not be considered to be all-inclusive, as it is not possible for a single document to cover all possible device changes. The question and answer sections cover the following types of changes:

- Manufacturing changes
- Labeling changes
- Technology or performance specification changes
- Materials changes

IV. Basic Principles

Certain principles of section 807.81(a)(3) affect the need to submit a 510(k) for a change to an existing device. The following basic principles underlie this guidance document:

⁴ See, for example, ODE Bluebook Memoranda [K86-3](#), [K90-1](#), etc., as well as device-specific guidance documents.

- Any person who is required to register under section 510 of the FD&C Act and 21 CFR 807.20 who plans to market a device for the first time (i.e., one that is not a modified version of a manufacturer's own already cleared device) is required to submit a 510(k).
- This draft guidance does not address medical devices that are exempt from 510(k) requirements under sections 510(l) or (m) of the FD&C Act. Changes to devices that are exempt from 510(k) requirements under those sections do not require 510(k) submissions unless the modified device exceeds the limitations of exemption described in section .9 of 21 CFR Parts 862-892 (i.e., 21 CFR 862.9, 21 CFR 864.9, etc.).⁵
- To determine whether a device modification is significant and thus requires a new 510(k), a manufacturer should compare the modified device to the most recently cleared version of that device and decide whether the modification could significantly affect the safety or effectiveness of the device. It follows from this basic principle that a number of comparisons are not relevant to the decision about submitting a new 510(k):
 - The modified device should not be compared to multiple devices, only to the most recently cleared version of that device, as described in that 510(k) submission.⁶
 - The modified device should not be compared to a version of the device that has not received clearance. In cases where a manufacturer has made several modifications to a device and judged that they do not require submission of a new 510(k), the modified device should be compared to the most recent version of the device that received 510(k) clearance, as it was described in that 510(k) submission.
 - The modified device should not be compared to any other device produced by the same manufacturer or another manufacturer, even if the other device could serve as a predicate to the modified device. The decision whether to submit a new 510(k) for a modified device is not based on whether the modified device is substantially equivalent to another device, it is based on whether the modification could significantly affect safety or effectiveness or whether it is a major change in the intended use of the device.

For example: A manufacturer produces two legally marketed devices; Device A has design A and is made of material A, Device B has design B and is made of material B. If the manufacturer modifies Device A to be made of material B, it would be inappropriate to assume that because material B is part of a different 510(k)-cleared device the modification does not require a new 510(k). It would also be inappropriate to compare the modified Device A with material B to any other legally marketed device to decide whether a new 510(k) is necessary, even if the other marketed device would be an obvious predicate device for purposes of determining substantial equivalence of the modified device.

⁵ FDA's regulations also contain exemptions from premarket notification requirements in 21 CFR 807.85. No premarket submissions is required for a device modification that falls within these exemptions.

⁶ Cleared 510(k) premarket notifications are listed in FDA's [510\(k\) database](#).

- A manufacturer should answer the questions posed below, in Sections V-IX, for *each individual change* to its device until a decision is made either to submit a 510(k) or to document the change and the basis for concluding that it does not require a 510(k). For instance, if a manufacturer changes the length of a device, the thickness of the device, and the material of the device, each of these three changes should be considered individually.
- Individual changes that do not require a new 510(k) may require one when evaluated collectively if those changes, taken as a whole, could significantly affect safety or effectiveness. After assessing each change individually, manufacturers should assess all changes made since the last 510(k) clearance collectively to determine whether the collective sum of all changes triggers the requirement for a new 510(k) submission.
- Whenever manufacturers change their device, they must comply with the Quality System (QS) regulation (21 CFR Part 820) unless the device in question is exempt from the QS regulation. This regulation requires that specification changes be documented, validated or, where appropriate, verified prior to their implementation.
- Manufacturers should have a mechanism or standard operating procedures in place for evaluating whether a proposed change meets the regulatory threshold for a new 510(k). Once a manufacturer has fully considered the device modifications:
 - If there are multiple changes and analysis of any one of the changes results in a determination that submission of a new 510(k) is required, then the manufacturer should submit a 510(k) that incorporates all of the planned changes as well as a comparison of the changed device to the device as it was described in the most recently cleared 510(k). All changes to the device since its most recent 510(k) clearance should be identified, even those that did not trigger the need for a new 510(k); the specific change(s) that triggered the 510(k) should be distinguished. Note that a table is often helpful for such comparisons.
 - If a manufacturer determines that its device modification(s) could not significantly affect safety or effectiveness and therefore decides not to submit a new 510(k), it should document the basis for concluding that it does not require a 510(k). Manufacturers should scientifically justify their conclusions that modifications, individually and collectively, could not affect safety or effectiveness. A copy of this documentation should be maintained. It is recommended that manufacturers answer each question below to satisfy basic Quality System requirements for documenting device modifications. *See 21 CFR 820.30 and 820.70(b).*

This guidance does not address every type of change to every type of device, and there will still be decisions in a "gray area" that manufacturers will have to make. For those circumstances where the proposed change is not addressed in this guidance or in a device-

specific guidance document, manufacturers are encouraged to contact the appropriate review divisions to obtain advice.⁷

Important Note on 510(k) Devices that Contain Nanomaterials or Otherwise Involve the Application of Nanotechnology⁸:

Nanotechnology is a new and evolving field for both the medical device industry and the Agency. At this time, FDA has not adopted nanotechnology-specific criteria to assist manufacturers in determining when a change to a device that contains nanomaterials or otherwise involves the application of nanotechnology rises to the level of significance that requires submission of a new 510(k). For this reason, FDA recommends that manufacturers consult with the agency for any nanotechnology-related changes to devices to determine whether and how the change may affect the safety or effectiveness of the device. FDA plans on developing additional guidance to further explain the Agency's thinking on this matter. Contact the appropriate review division with any questions on devices that contain nanomaterials or otherwise involve the application of nanotechnology.

V. Manufacturing Process Changes

Under 21 CFR 807.81(a)(3), a new 510(k) is required for a significant change or modification in manufacturing process that could significantly affect the safety or effectiveness of the device. The questions below address whether manufacturing changes constitute significant changes that would require a new 510(k), and provide examples of when a 510(k) is or is not required.

1. Was manufacturing process information part of the original 510(k) submission?

Manufacturing process changes will be particularly important for devices where the manufacturing process information was reviewed in the original 510(k) submission. Certain devices, such as contact lenses and wound dressings, typically involve review of manufacturing process information.⁹ Other devices may include manufacturing process information in the 510(k) in order to address specific concerns, and some devices may

⁷ See [CDRH Management Directory](#) or [CBER Key Staff Directory](#)

⁸ **Nanotechnology, Nanomaterial:** FDA has not adopted a formal definition of "nanotechnology," "nanomaterial," "nanoscale," or related terms. In the absence of a formal definition, FDA developed the following points to consider in determining whether a FDA-regulated product contains nanomaterials or otherwise involves the application of nanotechnology: (1) whether engineered substances have at least one dimension in the nanoscale range (approximately 1 nm to 100 nm); or (2) whether engineered substances exhibit properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer. Once finalized, the agency intends to apply these considerations broadly to all FDA-regulated products, including medical devices. For additional information, see FDA's draft guidance to industry titled "[Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology](#)."

⁹ See device-specific guidances for contact lenses and wound dressing devices, e.g., [Premarket Notification Document \(510\(k\)\) for Daily Wear Contact Lenses](#) and [Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Wound Dressing with Poly\(diallyl dimethyl ammonium chloride\) \(pDADMAC\) Additive](#).

undergo a pre-clearance inspection (e.g., infusion pumps – see [*Draft Guidance for Industry and FDA Staff - Total Product Life Cycle: Infusion Pump - Premarket Notification \(510\(k\)\) Submissions*](#)). In cases such as these, where manufacturing processes factor into the original clearance decision, the Agency has indicated that there is a higher likelihood that manufacturing process changes could significantly affect safety or effectiveness. Therefore, in cases where review of an original 510(k) submission includes a review of manufacturing process information, changes to manufacturing processes that could affect device specifications will likely require submission of a new 510(k). (Manufacturers should be aware of these requirements as they apply to their device type. Contact the appropriate review division with any questions.)

Device specifications include performance specifications (such as measurement accuracy), or physical or material characteristics (such as tensile strength). Changes to device specifications can significantly affect the performance of a device, and thus significantly affect a device's safety and effectiveness. Changes to these specifications may be unintended collateral changes. For example, a new manufacturing process might leave a residue on an implant and change the surface chemistry of the device, causing it to react differently to the *in vivo* environment, or a change in heat treatment of an alloy might significantly affect the alloy's physical properties, causing it to fail early.

2. Is there a change in packaging or expiration dating?

Generally, changes in device packaging or changes in the expiration date for use of a device do not result in the need to submit a new 510(k). Such changes are properly within the scope of the Quality System regulation. This conclusion is true whether the manufacturer applies an expiration date because of package integrity considerations, e.g., sterility, or because of a finite shelf-life of the device. However, where methods or protocols not described in the original 510(k) are used to support new package integrity or shelf-life claims, submission of a new 510(k) may be necessary. When such methods or protocols are described in the original 510(k), FDA reviewers should evaluate them with possible future use of the method or protocol in extended testing in mind.

3. Has there been a change in sterilization?

Changes in sterilization have the potential for changing the performance characteristics of a device. If these changes could significantly affect the safety or effectiveness of the device, the changes in sterilization methods trigger the requirements for a 510(k) submission. When manufacturers make changes in sterilization methods, they should document that the important properties and specifications of the device remain unaffected as part of their compliance with the QS regulations. In addition, if the sterility assurance level (SAL) is changed, manufacturers should consider whether device safety or effectiveness may have been compromised by the new level. If the SAL remains better than 10^{-6} , a new 510(k) submission is not necessary; only if the SAL is less than 10^{-6} should a 510(k) be submitted. Changes to the sterilization method, such as changing from moist heat sterilization to e-beam radiation, require a new 510(k). Changes that result in a device being provided non-sterile when it was previously provided sterile, or vice-versa, also warrant a new 510(k).

VI. Labeling Changes

Changes in device labeling often pose the most difficult questions to be addressed by device manufacturers when deciding whether a new 510(k) submission is necessary. Frequently, an apparently subtle change in a device's labeling can have a significant impact on the safe and effective use of the device.

In order to properly consider labeling changes, it is important to keep in mind that the term "labeling" includes more than just the instructions for use. According to the FD&C Act, labeling means all written, printed, or graphic matter on or accompanying a medical device.¹⁰ Labeling can therefore include things such as instructions that are displayed on a screen by software, stickers or text placed on a control unit, and promotional materials.

We recommend that manufacturers consider the following questions to determine whether a labeling change requires submission of a new 510(k):

1. Does the change affect the indications for use?

For the purposes of this discussion, "indications for use" refers to a description of the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient for which the device is intended.¹¹ FDA views most labeling changes that affect the indications for use, as just described, whether made to a specific indications section of the labeling or not, as major changes to the intended use of a device that warrant the submission of a 510(k).

FDA would not consider a change in the indications for use that removes certain indications or limits use within the currently cleared indication *due strictly to marketing reasons* to be a major change in intended use under 21 CFR 807.81(a)(3) that requires submission of a new 510(k). For example, if a device was cleared for use with three indications and the firm decides to market the device for only two of those indications due to changes in market demand, FDA generally would not consider this to be a "major change" under the rule that would require submission of a new 510(k). However, if a firm decides to market the device for only two of those indications due to other reasons, for example, changes that have been made to the device that affect the removed indication or because of complaints or corrective actions, FDA would generally consider the removal of the indications for use to be a "major change" that requires a new 510(k).

Four other common labeling changes that affect the indications for use and that FDA believes would usually require submission of a 510(k) are:

- Changes that allow reuse of devices previously labeled "single use only"
- Changes from prescription to over-the-counter (OTC) use

¹⁰ §201(m): "The term 'labeling' means all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."

¹¹ The term indications for use is defined in the PMA regulation at 21 CFR 814.20(3)(i). We have applied the definition in the same way in the 510(k) context.

- Changes from prescription use in a clinical setting to prescription use in a home setting (home use devices¹²)
- Changes from general patient populations to specific patient populations (e.g., changes from an undefined patient age group to a pediatric population)

2. Does the change affect the contraindications for use?¹³

a. Does the change add a contraindication?

While all changes in the labeled contraindications for device use should be reviewed by the Agency, FDA recognizes that, in general, the addition of a contraindication based on new information is important to public health and should be implemented immediately. To facilitate the timely implementation of such changes, manufacturers are encouraged to add new contraindications to labeling of cleared devices and to notify existing device users of such contraindications as expeditiously as possible whenever a pressing public health need arises. The new labeling should be submitted to FDA as part of a new 510(k) that is prominently labeled “change being effected” (CBE). Manufacturers may market the device with the modified labeling unless otherwise notified by FDA (FDA may ask for revisions during review of the 510(k)).¹⁴ Manufacturers should be thoroughly familiar with what constitutes a true contraindication to make a change effective before clearance; if there are any questions, contact the Agency before proceeding.

b. Does the change delete a contraindication?

Manufacturers planning to delete a contraindication should submit a new 510(k) prior to effecting the change because this type of labeling change expands the indications for use. For example, if a physical restraint was contraindicated for use with individuals weighing less than 100 pounds and the manufacturer subsequently wishes to remove this contraindication, a 510(k) should be submitted and cleared prior to marketing the device with the new labeling.

3. Is it a change in instructions for use?

If the labeling change instructs the user to use the device in a different fashion from that originally cleared, then this could lead to new significant safety risks or less effective use of

¹² For purposes of this guidance, FDA considers a home use device to be a medical device intended for users in a non-clinical environment that is managed partly or wholly by the user. These devices require adequate labeling for the user and may require training for the user by a licensed health care provider. Please see <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/HomeHealthandConsumer/HomeUseDevices/default.htm>.

¹³ Contraindications describe populations in whom or situations in which a device should not be used because the risk of use clearly outweighs any reasonably foreseeable benefits. See the Blue Book Memorandum G91-1, [Device Labeling Guidance](#).

¹⁴ Note that FDA considers the addition of new contraindications to be a major change in intended use that requires submission of a 510(k). Before submission and clearance of a 510(k), the device with the changed intended use is adulterated under § 501(f)(1)(B) of the FD&C Act and misbranded under § 502(o) of the FD&C Act. However, FDA intends to exercise enforcement discretion with regard to these violations where manufacturers immediately implement a change in contraindications in order to protect the public health, as long as a new 510(k) labeled “change being effected” is submitted to FDA concurrently.

the device. FDA views changes of this nature as major changes in intended use that require submission of a 510(k). Such changes are likely to significantly affect safety or effectiveness and therefore should generally be reviewed by the Agency in a 510(k) prior to marketing. Note that changes in instructions may or may not also constitute changes in indications for use.

Examples:

- Labeling for a device that provides diagnostic information is modified to include additional or new instructions on how to interpret data from the device. FDA considers this change a major change in intended use that could significantly affect the treatment of the patient and that requires submission of a 510(k).
- Labeling for a cutting instrument or laser is modified to include additional or new instructions about incision procedures. FDA considers this change a major change in intended use that could significantly affect the safety and effectiveness of the device's treatment of the patient and that requires submission of a 510(k) prior to marketing.

4. Is it a change in warnings¹⁵ or precautions?¹⁶

Manufacturers should monitor device usage to facilitate continuous upgrades of device labeling and promptly revise the warnings and precautions sections based on use experience. Events that precipitate changes of this type should be reported under the Medical Device Reporting regulation (MDR), 21 CFR Part 803. Submission of a new 510(k) for labeling changes that add warnings or precautions is generally unnecessary; however, manufacturers are encouraged to discuss these situations with FDA. Labeling changes that delete warnings or precautions, however, could be changes in intended use that affect how a device is used and could therefore have a significant effect on safety or effectiveness. These changes are likely to warrant new 510(k) submissions.

5. Is it some other labeling change?

Other types of labeling changes might include clarifications to language that do not change the meaning, aesthetic or organizational changes to the way information is displayed, or logo or name changes. These types of changes are not usually considered major changes to the intended use and will not typically require a new 510(k). For example, the instructions for use of an automated clinical chemistry analyzer may be modified to clarify how routine batch testing operation may be temporarily interrupted to allow efficient processing of high priority samples.

¹⁵ Warnings describe serious adverse reactions and potential safety hazards along with consequent limitations in use and mitigating steps to take if they occur. See the Blue Book Memorandum G91-1, [Device Labeling Guidance](#).

¹⁶ Precautions describe any special care to be exercised by a practitioner or patient for the safe and effective use of a device. See the Blue Book Memorandum G91-1, [Device Labeling Guidance](#).

VII. Technology, Engineering, and Performance Changes

To determine whether a technology, engineering, or performance change requires a new 510(k), manufacturers should first review the labeling questions above, as technology changes sometimes affect device labeling, then review the following questions. Even if labeling has not been affected, a new 510(k) submission should generally be submitted for modifications to device technology, engineering, and performance that significantly affect the cleared Indications for Use or fundamental technology of the existing device, or that substantially change the performance characteristics or specifications of the device. These types of modifications encompass a broad span of changes, from minor engineering changes in a circuit board layout to a change from electromechanical to microprocessor control of device function.

Although the examples provided under each question below generally refer to specific device types, these examples are intended to be pertinent to similar types of changes involving different devices.

1. Does the change alter the fundamental scientific technology of the device?

The fundamental scientific technology of a medical device encompasses both the design principle – the underlying scientific principle by which the device performs its intended therapeutic or diagnostic function – and the method by which that principle is applied. While many changes to the technology and design of a medical device discussed in this section of the guidance do not trigger the requirement for a new 510(k), all changes in fundamental scientific technology could significantly affect safety or effectiveness. Therefore, such changes require the submission of a new 510(k).

Examples:

- A humidifier is designed to add moisture to the air. The design principle of such devices is that water droplets must be separated and dispersed in order to add moisture to the air. Two applications of this principle that achieve the intended use are (1) vibrating piezoelectric material under a quantity of water (separation and dispersion of water molecules by high frequency vibration), and (2) using a wick to spread water, and a fan to disperse water droplets over a wide surface area such that an adequate threshold of airflow can disperse the molecules. These two mechanisms use the same design principle, but apply it in different ways. A device modification from one application mechanism to the other could significantly affect safety and effectiveness, and should therefore result in a new 510(k) submission.
- A device is changed from analog to digital control. This change is considered a change in the fundamental scientific technology of a device. While the change to digital control can markedly improve device performance specifications and effectiveness, the integration of a digital control into a previously all-analog system is complex and usually undertaken only as part of a major redesign of a product that could significantly affect safety or effectiveness. Thus, a new 510(k) should be submitted prior to marketing.

- A manufacturer of a computed tomography x-ray system who changes the image reconstruction algorithm from simple back projection to a new, modified method is changing the fundamental scientific technology of its device. This type of change could significantly affect safety and effectiveness and should therefore be reviewed in a new 510(k).
- A manufacturer wants to modify the component of a hemodialysis delivery system that is responsible for maintaining the fluid balance of the dialysis treatment (i.e., the amount of fluid that is removed and returned to the patient). Because this change could directly impact the safety or effectiveness of the fluid balancing algorithm, and therefore the safety or effectiveness of the treatment, a new 510(k) should be reviewed prior to marketing.

2. Is it a change in energy type?

Energy type refers to the type of power input to or output from the device. Changes in energy type are a change in design that will always have a significant effect on safety or effectiveness because power inputs and outputs are typically critical to proper device function. Most of these changes should be reviewed in a new 510(k) prior to marketing.

Examples:

- A device that is changed from an external power source to battery power should result in submission of a new 510(k).
- A device that is modified to use radiofrequency (RF) energy instead of microwave energy, for instance, in an ablation device changes how the device functions and could significantly affect safety and effectiveness. (This change could also be considered a change in fundamental scientific technology.) This change should result in a new 510(k) submission.

3. Does the change have the potential to significantly alter the performance characteristics or specifications of the device?

Such changes directly impact the performance, and potentially the safety and effectiveness, of the device and a new 510(k) with comparative testing should be provided for such modifications, whether the performance characteristics are improved or worsened.

Examples:

- A currently marketed pulse oximeter is only sensitive to an oxygen saturation of 90%, and a manufacturer wants to modify the device to be sensitive down to a concentration of 70%. While this change is an improvement in the device's capabilities, the performance specifications of the device are being altered, which could significantly affect safety or effectiveness. A new 510(k) submission should be provided.

- A manufacturer modifies a hemodialysis catheter to make the device more flexible and kink-resistant. Even though these changes are intended to increase the safety and effectiveness of the device, the modifications potentially alter the performance characteristics and safety and effectiveness of the device and therefore a new 510(k) should be submitted.
- A manufacturer wants to modify its immunoassay from monoclonal to polyclonal (or vice versa) or to recombinant monoclonal to improve performance. This change could significantly affect safety or effectiveness so a new 510(k) should be submitted.

4. Is it a change in ergonomics or the patient/user interface?

Changes of this type may significantly affect the safety or effectiveness of the device, but not all such changes do. The factors to consider in determining whether such a change requires submission of a new 510(k) are whether the change can expand how the device will be used or affect how it will perform. Changes that are made only to increase comfort and could not result in a corresponding improvement (or decline) in safety and effectiveness are unlikely to warrant a new 510(k); however, one must consider how each of these changes might affect safety or effectiveness. Simple design changes may have unintended consequences, as illustrated by the first example below.

Examples:

- A surgical handpiece handle is modified to make the device less bulky and easier to wield by relocating the motor closer to the proximal end of the device. While this change may be intended to increase user comfort, the motor could be too close to the treatment area on the patient or to the user's hand and cause burns, or the mechanical performance of the device could be affected. Since this change could significantly affect the safety or effectiveness of the device, a new 510(k) should be submitted.
- The device handle of an endoscopic suturing device is modified to change the molded shape to a more ergonomic design, rounding square corners for physician comfort. Only the handle is modified and the functional portions of the device remain unchanged. This ergonomics change is unlikely to significantly affect safety or effectiveness. FDA would not expect a new 510(k) in this instance.
- A mask used for CPAP (continuous positive airway pressure) is modified to use a new, softer material for increased patient comfort. Since this change could affect the fit of the mask on the patient's mouth and the pressure used to keep the airway open for unobstructed breathing, safety and effectiveness could be significantly affected, and a new 510(k) should be submitted.
- A manufacturer wants to change a coded calibrator glucose meter to a "no code" glucose meter, i.e. a factory calibrated meter, eliminating the need for the patient to calibrate the device. This patient/user interface change could significantly affect the safety or effectiveness of the device, and a new 510(k) should be submitted in this instance.

- The interface of a dental surgical unit is modified to improve the display of treatment parameters in an effort to improve communication of information during treatment. While such a change could affect the safety and effectiveness of the device, the Agency would not generally consider this change significant, and therefore would not expect a new 510(k).

5. Is it a change in dimensional specifications?

Dimensional changes can, but do not always, significantly affect safety and effectiveness. Whether or not they will depends on the device type and the component being modified. For example, the dimensions of the casing of a typical ventilator unit do not significantly affect the safety or effectiveness of the device, however, the length of the ventilator hose is directly related to the effectiveness of the device as a longer hose will require higher pressure to circulate air. FDA recommends that manufacturers consult the appropriate review division regarding any questionable dimensional change. Typically, dimensional changes that change a device dimension that is related to the performance of the device outside of the cleared dimensional tolerance range have the potential to significantly affect safety or effectiveness. For instance, if a device is cleared with a length of $10.0\text{ mm} \pm 0.5\text{ mm}$, a modification that makes the length 10.5 mm would not be significant (please note that a second change that makes the length 11.0 mm would be outside the tolerance range of the originally cleared device and thus be significant). Device dimensions that are modified beyond tolerance ranges will usually warrant a new 510(k), although modifications within previously cleared size ranges typically will not (see second example).

Examples:

- A biliary stent is modified to have a longer length (outside of its dimensional tolerance range). The length (or diameter) of a biliary stent is an essential characteristic of the device, and even a small change can significantly affect the safety or effectiveness of the device, even if it is in between currently marketed sizes. Therefore, a new 510(k) should be submitted for this change.
- A manufacturer of a bone plate whose last 510(k) included 2 and 4 mm thick variations introduces a 3 mm thick version of an otherwise identical plate. This modification would not require a new 510(k), as no new risks are being introduced. (However, a new version of the bone plate that is outside the cleared 2-4 mm thickness range may introduce new risks and should therefore result in a new 510(k) submission.)
- The case of an infusion pump is increased in size in order to facilitate a larger display panel. The size of the internal pump mechanism is not modified. This change is not likely to significantly affect the safety or effectiveness of the device because the modified dimension is not directly related to the performance of the device, and therefore the manufacturer does not need to submit a new 510(k).

6. Is it a change in software or firmware?

Small changes to device software – including software that is an integral part of a device or stand-alone software that constitutes a medical device in and of itself – can have pervasive effects on the safety or effectiveness of a device and trigger the need for a new 510(k) submission. However, some low risk changes may be made by following the QS regulation (including design controls) and documenting the appropriate validation testing. The factors to consider in determining whether such a change requires a new 510(k) are whether the software change could expand the capability of the device or affect device performance. Such changes will likely warrant a new 510(k). Changes to device software that could affect a clinical algorithm (an algorithm that controls how software analyzes, interprets, or uses patient data) would also warrant a new 510(k).

Examples:

- Software that plans placement of an implant based on patient case data is modified to plan placement of different implants or to plan placement based on a new patient parameter. These changes should result in a new 510(k).
- Software for a dental operative unit is modified to allow for use of a new control feature. This change should result in a new 510(k).
- Software for an electroencephalograph (EEG) is configured to display a generic error message when a sensor is disconnected. The software is modified to display a more specific error message that instructs the user to connect the disconnected sensor. This change does not significantly affect the safety or effectiveness of the EEG and does not require a new 510(k).
- The software for a polysomnogram (PSG) is modified to allow for saving or printing of recorded information for post-acquisition viewing. This change does not significantly affect the safety or effectiveness of the PSG and does not require a new 510(k).

7. Does the modification impact how the device receives, transmits, or displays electrical signals or data?¹⁷

While such changes may seem innocuous, most changes of this nature have the potential to significantly impact safety or effectiveness by altering data communication quality and therefore should result in a new 510(k) submission. Also see [Deciding When to Submit a 510\(k\) for a Change to an Existing Wireless Telemetry Medical Device.](#)

Examples:

¹⁷ Note that Medical Device Data Systems (MDDS) are exempt from 510(k) requirements, see 21 CFR 880.6310, and are outside the scope of this draft guidance. For more information on MDDS, see <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/GeneralHospitalDevicesandSupplies/MedicalDeviceDataSystems/default.htm>.

- Diagnostic software that typically displays images on a monitor in a clinical setting is modified to output the image to a portable hand-held device that can be used to view the images from any location. This change could result in new risks, such as the inability to discern certain data due to a smaller hand-held screen, lower picture resolution, or loss of data during transmission, that could significantly affect the safety and effectiveness of the software. Therefore, this change should result in a new 510(k) submission.
- An infusion pump that was cleared with a hard-wired connection to a keyboard to input treatment parameters is modified to include wireless capability to allow for remote input of treatment parameters. This change could significantly affect safety or effectiveness by altering data communication quality, which could affect the input of treatment parameters, and should therefore result in a new 510(k).

8. Is the modification intended to add an aspect of autonomous or semi-autonomous control to the existing device?

Any device modification that takes control of the device away from the user or is used to assist or take away decision-making from a user likely introduces new risks that could significantly affect safety or effectiveness, and should be reviewed in a new 510(k) submission prior to marketing.

Examples:

- A colon imaging software package is modified to include computer assisted detection to assist the physician in determining potentially malignant tissue. As a new feature, this change could significantly affect the safety or effectiveness of the device by introducing the possibility of false positives or negatives that could adversely affect the course of treatment. This change requires a new 510(k).
- A dental handpiece is modified to automatically increase or decrease the revolutions per minute (rpm) of a drill bit based on treatment selected or the type of bone encountered. Automating this treatment parameter introduces several new risks, such as an inappropriate automatic increase to an unsafe rpm or an inappropriate automatic decrease to an ineffective rpm. These risks constitute significant effects on safety and effectiveness. This change requires a new 510(k) prior to marketing.
- A device that acquires nerve conduction waveforms and extracts multiple parameters from those waveforms is modified to include software that automatically compares the parameters to a reference database to provide a diagnosis. An automated diagnosis can influence patient treatment and could significantly affect the safety and effectiveness of the device. This change requires a new 510(k).

9. Is the change being implemented to address a specific risk or failure mode for your device?

Changes that are implemented to address either known or newly identified safety risks or failure modes of a device, including those intended to address a known device- or user-

related adverse event or complaint, are by definition likely to significantly affect safety or effectiveness, even if the modification is intended to make the device more safe than the previous version. These modifications may include the implementation of new alarms or new alarm setpoints, modifications to the user interface to display new information that may be used to manage device settings, or design modifications that are intended to eliminate known failure modes. These changes should usually result in new 510(k) submissions.

These situations may also call for a device recall. You should contact the CDRH Office of Compliance or the Office of Compliance and Biologics Quality in these cases, and if a recall is initiated, consult the Blue Book Memorandum K95-1, [*510\(k\) Requirements During Firm-Initiated Recalls*](#).

Examples:

- A manufacturer of a fluid warming device wants to add a protective mechanism (either hardware or software) to cut off power to the device should the fluid temperature increase past a certain setpoint. This change also addresses a specific risk, and could significantly affect safety or effectiveness. This change should result in the submission of a new 510(k).
- A manufacturer wants to add a color-coded luer or proprietary connector to address the risk of misconnections for a feeding tube. A change of this type should result in the submission of a new 510(k).

10. Does the change affect how the device is likely to be used in practice?

Technological or design changes may affect how a device is used in practice, and therefore affect the safety or effectiveness of the device, even if no change in the Indications for Use statement accompanies the change. Such changes may create the need for new directions for use or a limitation in the device labeling to address the potential that an off label use could cause harm.¹⁸ Particularly when the modification could create a reasonable likelihood of off-

¹⁸The FD&C Act provides in section 513(i)(1)(E)(i) that:

Any determination by the Secretary of the intended use of a device shall be based upon the proposed labeling submitted in a report for the device under section 510(k). However, when determining that a device can be found substantially equivalent to a legally marketed device, the director of the organizational unit responsible for regulating devices (in this subparagraph referred to as the "Director") may require a statement in labeling that provides appropriate information regarding a use of the device not identified in the proposed labeling if, after providing an opportunity for consultation with the person who submitted such report, the Director determines and states in writing—

(I) that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device; and

(II) that such use could cause harm.

FDA would make such a finding in writing where it determines that such a change is reasonably likely to result in an off-label use that could cause harm.

label use that could cause harm, a new 510(k) should be submitted to allow FDA to determine whether a change to the labeling is necessary, even if the manufacturer does not intend a change to the indications for use in the labeling. The questions below are intended to guide manufacturers in determining whether changes to device technology, engineering, or performance constitute significant changes that trigger the need for a new 510(k) to enable FDA to evaluate whether “appropriate information” in the labeling about a use not currently identified in the labeling is necessary.

a. Is the modification to the device likely to alter or expand the use of the device?

If an existing device is being modified to allow for its use in a different or modified type of medical procedure, or to treat or diagnose a disease or medical condition apart from what has been previously cleared, the potential to significantly affect safety or effectiveness will be high, and therefore, these changes should result in a new 510(k) submission.

Examples:

- A manual surgical instrument is modified so that it can be connected to an electrical stimulator and conduct current (i.e., is now both a surgical instrument and an electrode). This change should be submitted in a 510(k) prior to marketing.
- The length of a surgical scissor is modified such that an existing device previously intended for only open surgical procedures can now be used for closed, endoscopically-controlled procedures. This change should be submitted in a 510(k) prior to marketing. (Note that while a typical surgical scissor is exempt from submitting a 510(k) by regulation, 21 CFR 878.4800, a 510(k) submission may be necessary in this instance because the change may alter the intended use of the device or may involve a different fundamental scientific technology than the generic type of device (21 CFR 878.9(a), (b)).)
- An in vitro diagnostic test is modified such that the processing utilizes frozen biopsy tissue samples rather than paraffin embedded tissue samples, so that users have more flexibility in tissue processing. This change could significantly affect the device performance and therefore should be submitted in a 510(k) prior to marketing.

b. Does the modification allow for the use of the device in a new, expanded, or more specific patient population?

Design changes that allow use in a new, expanded, or more specific patient population also carry a high potential to significantly affect safety or effectiveness, and therefore, these changes should result in a new 510(k) submission.

Examples:

- New features of a ventilator allow the device to be used for the treatment of pediatric patients, whereas previously it was only cleared for use by patients who had a tidal volume in the adult range. This is an example of an expanded patient population that should result in a new 510(k).
- The dimensional specifications of a feeding tube are reduced to facilitate use of the device in an infant by making the implanted portion shorter and the tubing diameter smaller and thus more appropriate for the slower flow rate and volume necessary for use of the device in an infant. This is an example of a more specific patient population which should result in a new 510(k).
- An evoked response auditory stimulator intended to aid in the detection of lesions in the auditory pathway for the general population is modified in order to detect lesions in a specific patient population, e.g., persons identified as having a higher level cognitive dysfunction thought to be related to hearing. This is an example of a device being modified for a more specific patient population. This modified device should be reviewed in a 510(k) prior to marketing.

c. Does the modification significantly change or alter an established medical procedure associated with the device?

Changes that result in an alteration to an established medical procedure should be reviewed in a new 510(k) prior to marketing because the new use of a device may introduce new safety risks or lead to less effective use of the device.

Example:

- Components of a surgical kit are combined with a surgical handpiece to allow cricothyroidotomy to be performed with one device. This device modification and its corresponding modified procedure could significantly affect the safety or effectiveness of the device and therefore should result in a new 510(k).

d. Is a specific modification intended to allow for the use of the device in a new environment in which there may be new risks affecting safety and effectiveness?

In general, modifications to allow a device to be used in a new environment are associated with new risks. Therefore, in most cases, changing a device to fit a new environment should result in a new 510(k) submission.

Examples:

- A stationary electrocardiogram (ECG) device originally cleared and intended for use in hospitals is modified to reduce lead sets or incorporate modular electrodes, which may allow use in pre-hospital settings such as ambulance transport. This change should result in a new 510(k) submission prior to marketing.
- If an electroencephalograph (EEG) seizure detection device originally intended for use in post hoc review of EEG data from epilepsy monitoring units is modified to add a real-time alarm, it may allow use in an intensive care setting.

Similarly, if an EEG device originally intended for general use is modified to reduce the number of electrodes, it may allow use in emergency settings. These changes would introduce new risks and therefore should be reviewed under 510(k) prior to marketing.

e. Is the change intended to allow the device to be used by a lay person outside of a clinical setting?

These changes may include those that change the indication of the device from prescription to over-the-counter, as well as those that allow the device to be used by a lay person outside of a clinical setting as prescribed by a physician (home use). Both types of changes introduce new risks that could significantly affect safety or effectiveness, and therefore should result in the submission of a new 510(k).

Examples:

- An ECG device is modified to reduce the number of leads or simplify electrode placement to allow for home use or over-the-counter use. This change should result in a new 510(k) submission prior to marketing.
- A hemodialysis machine is modified to incorporate additional safety features, a more friendly user interface, and a special user's manual so that it may be operated by a lay person. The potential for use by a lay person outside the clinical setting introduces new risks. This change should be reviewed in a new 510(k) submission prior to marketing.

f. Does the modification allow for the device to provide new information or data to the user that could be used for patient assessment or diagnostic purposes?¹⁹

New technological characteristics that allow use for patient assessment or diagnostic purposes could significantly affect the safety or effectiveness of a device and may necessitate a new 510(k). This principle applies even if the new patient assessment information is used as an aid or adjunct to other measures or is only considered additional information.

Examples:

- A device that previously only qualitatively displayed blood flow or stenosis by displaying an image is modified to output quantitative or semi-quantitative data for these assessments. This change from qualitative, or informational, data to quantitative data would introduce new risks for the device and significantly impact safety and effectiveness. A new 510(k) should be provided.

¹⁹ For the purposes of this guidance, any device that provides data or information used to assess a patient's condition or treatment can be considered diagnostic. A device need not be indicated solely for screening or providing diagnoses to be considered diagnostic.

- A device that previously only derived four parameters from an EEG waveform is modified to derive two additional parameters from the waveform. This change should result in a new 510(k).
- A device that previously calculated four parameters from a waveform is modified to calculate a standard deviation or variance of those parameters to aid in detecting abnormalities of the waveform as a diagnostic tool. This change should be reviewed in a 510(k) prior to marketing.
- A device cleared only to acquire and display raw physiological data is modified to include software that automatically analyzes, interprets, highlights or extracts parameters from the physiological data. This change should result in a new 510(k) prior to marketing

VIII. Materials Changes

Firms making changes to the materials from which their device is manufactured should first consider the other types of changes discussed above and their impact on the decision regarding the need for submission of a new 510(k). For example, a change of material type might also engender a change in the labeling of the device (e.g., the removal of a contraindication or addition of a warning) or a change in performance specifications (e.g., a reduction in tensile strength). These collateral changes should be considered first.

The first consideration for devices undergoing a modification to the device material is whether the material contacts the patient. Patient-contact includes both direct and indirect contact, whether of very transitory or permanent duration. In general, material modifications to device components that cannot have direct or indirect contact with the patient do not significantly affect safety or effectiveness of the device and so do not require a new 510(k) submission, unless they affect the fundamental device technology or performance (e.g., preservatives, antibacterials, moving parts, structurally significant components, lubricants, etc.).

Direct contact is when a material touches any tissue or bodily substance of a patient while it is still in or on a patient. Indirect contact is when a material has the *potential* to come into contact with any patient tissue or bodily substance by some intervening material (such as a liquid or gas) by first coming in contact with the intervening material, which subsequently comes in contact with the patient tissue or bodily substance. For example, a catheter hub (the part of the catheter which is external to the patient) contacts the patient indirectly. Fluids and drugs are infused through the hub and directly into the patient and, therefore, materials in the hub should demonstrate biocompatibility.

While most implants contact patients directly, there are some exceptions that have materials that are not considered patient-contacting. An example is a spinal cord stimulator. The internal contents of these devices are not patient-contacting; they are hermetically sealed so that there is no material transfer, fluid transfer, or leaching out of any material internal to the device. The internal components do not need to demonstrate biocompatibility.

1. Is it a change in material formulation?

Material formulation includes the chemical composition of the material, including the ratio of constituents and ingredients and their interactions, and their related physical chemistry.

It is important to keep in mind that material formulation can be affected by the processing aids, catalysts, and residual contaminants that are not intended to be a part of the material but may be introduced by manufacturing, sterilization, or handling. Changes to these processes may indirectly result in changes to material formulation.

a. Does the change affect patient-contacting materials (either direct or indirect)?

Changes in material formulation of patient-contacting devices or device components may affect the biocompatibility of the device. These changes may also affect material properties and the safe and effective performance of a device. Therefore, a new 510(k) should be submitted for changes in material formulation for patient-contacting devices or device components.

While it is conceivable that material formulation changes that do not affect patient-contacting materials could impact the safety or effectiveness of a device, this outcome is not typical. For most material formulation changes of non-patient-contacting materials, it is appropriate to simply document the change.

2. Does the change involve the device surface?

Changes to a device coating or surface modification technique, including chemical formulation, method of application, or surface preparation (e.g., acid-etching, blasting, etc.) generally significantly affect safety or effectiveness and would require a new 510(k). Keep in mind that residual contaminants from manufacturing, sterilization, and other processes can indirectly change the device surface.

IX. Is clinical data necessary to determine substantial equivalence?

A manufacturer's determination that clinical data is needed because bench testing or simulations are not sufficient to assess the safety or effectiveness of a modified device is a sure sign that the modification could significantly affect safety or effectiveness and that a new 510(k) should be submitted. Note that this criterion does not necessarily apply to in vitro diagnostic devices, which have different testing requirements. Contact the appropriate review division within the Office of In Vitro Diagnostics if you have questions.

For the purposes of this guidance, clinical data is not only data acquired from prospective, controlled clinical trials but includes any data derived from human subjects.